

**Amendments to the Claims:**

The listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A method for testing *Streptococcus pneumoniae* for resistance to penicillin, the method comprising the steps of:

- a) isolating DNA from *Streptococcus pneumoniae* having unknown resistance to penicillin,
- b) hybridizing the DNA obtained in step (a) with
  - (i) at least one DNA probe that specifically hybridizes specific to a DNA sequence specific to a penicillin binding protein (PBP) gene of penicillin sensitive strains of *Streptococcus pneumoniae*, wherein the DNA sequence is present in the PBP gene of penicillin sensitive strains of Streptococcus pneumoniae but is modified in the PBP gene of penicillin resistant strains of Streptococcus pneumoniae; and
  - (ii) at least one DNA probe that specifically hybridizes specific to a DNA sequence specific to a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae*, wherein the DNA sequence specific to a PBP gene of penicillin resistant strains of Streptococcus pneumoniae is different from the DNA sequence of the PBP gene present n penicillin sensitive strains of Streptococcus pneumoniae, and
- c) determining whether or not said *Streptococcus pneumoniae* is sensitive to penicillin or not by detecting which probe or probes hybridize,

wherein the PBP gene is selected from the group consisting of PBP2x, PBP1a and PBP2b.

2. (Cancelled)

3. (Currently Amended) The method according to claim [[2]] 1, wherein the DNA sequence of at least one DNA probe ~~that specifically hybridizes~~ specific to a DNA sequence specific for a PBP gene of penicillin sensitive strains of *Streptococcus pneumoniae* consists of a DNA sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13.

4. (Cancelled)

5. (Currently Amended) The method according to claim [[4]] 1, wherein the DNA sequence of at least one DNA probe ~~that specifically hybridizes~~ specific to a DNA sequence specific for a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae* consists of a DNA sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18 and SEQ ID NO: 19.

6. (Original) The method according to claim 1, wherein the probes are labeled radioactively.

7. (Cancelled)

8 (Currently Amended) The method according to claim 1, wherein DNA obtained in step (a) is hybridized with more than one DNA probe ~~that specifically hybridizes~~ specific to a DNA sequence specific for a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae* and more than one DNA probe ~~that specifically hybridizes~~ specific to a DNA sequence specific for a PBP gene of penicillin sensitive strains of *Streptococcus pneumoniae*.

9. (Currently Amended) The method according to claim [[2]] 1, wherein DNA obtained in step (a) is hybridized with more than one DNA probe ~~that specifically hybridizes specific~~ to a DNA sequence specific for penicillin a PBP gene of sensitive strains of *Streptococcus pneumoniae* chosen from among said group.

10. (Currently Amended) The method according to claim [[4]] 1, wherein DNA obtained in step (a) is hybridized with more than one DNA probe ~~that specifically hybridizes specific~~ to a DNA sequence specific for a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae* chosen from among said group.

11. (Currently Amended) A method for testing *Streptococcus pneumoniae* for resistance to penicillin, the method comprising the steps of:

- a) isolating DNA from *Streptococcus pneumoniae* having unknown resistance to penicillin,
- b) exposing the DNA obtained in step (a) with at least one DNA probe ~~that hybridizes specific~~ to a DNA sequence specific for penicillin sensitive strains of *Streptococcus pneumoniae* and at least one DNA probe ~~that hybridizes specific~~ to a DNA sequence specific for penicillin resistant strains of *Streptococcus pneumoniae* under conditions that would permit hybridization, and
- c) determining whether or not said *Streptococcus pneumoniae* strain is sensitive to penicillin or not by detecting which probe or probes hybridize; wherein the at least one DNA probe ~~that hybridizes specific~~ to a DNA sequence specific for penicillin sensitive strains of *Streptococcus pneumoniae* is selected from the group of sequences consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID

NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13 ~~and sequences that differ from these sequences by one to four nucleotides; and wherein the at least one DNA probe that hybridizes specific to a DNA sequence specific for penicillin resistant strains of *Streptococcus pneumoniae* is selected from the group of sequences consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19 ~~and sequences that differ from these sequences by one to four nucleotides.~~~~

12. (Cancelled)

13. (Cancelled).

14. (Currently Amended) The method of claim 11, wherein DNA from said *Streptococcus pneumoniae* is exposed to more than one different DNA probe ~~that hybridizes specific to a DNA sequence specific for penicillin sensitive strains of *Streptococcus pneumoniae* is a DNA sequence consisting of a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13 ~~and sequences that differ from these sequences by one to four nucleotides, under conditions that can permit hybridization; and,~~~~

wherein DNA from said *Streptococcus pneumoniae* is exposed to more than one different resistance-specific DNA probe selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17; SEQ ID NO: 18, and SEQ ID NO: 19 ~~and sequences that differ from these sequences by one to four nucleotides, under conditions that can permit hybridization.~~

15. (Withdrawn) A penicillin sensitivity-specific DNA probe for determining penicillin sensitivity in *Streptococcus pneumoniae* selected from the group of sequences consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3,

SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13 and sequences which differ from said sequences by one to four nucleotides, wherein SEQ ID NOS.: 1-13 are, respectively:

AGT CAG CAA CGG GTA AG,

AAC GAA CGA TGG ACG GT,

CAT TTC CAG NCC CCT CCA,

TGC AGA TGC CAC GAT TC,

CTG GTC AGC TTC CTG CG,

TGG TTA TCT AGT CGG GTT AA,

CTG TAT CGA TGA GTC CG,

AAC AGT TCT GCT GAA GAA G,

TAG GAG CAC GCC ATC AGT,

GAC GAA ATG CCT ATC TTG,

CTC TCA ATT TGT AGC ACC T,

CTA TTC TAA CCG TCT GAC A, and

ATC AAA TAC CTA TAT GGT CC;

wherein N is any nucleotide.

16. (Withdrawn) A penicillin resistance-specific DNA probe for determining penicillin resistance in *Streptococcus pneumoniae* selected from the group of sequences consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID

NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19 and sequences which differ from said sequences by one to four nucleotides, wherein SEQ ID NOS.: 14-19 are, respectively:

TGG AGA ATA NTT CAA TAG N,

GTC TAC TTG AAC AAA AAA TG,

TTA GTT GGG ACG GAC CCT,

GTA ACN NTT CAA CAG CCT,

CTC CGA NCA ATA CGT CTC T, and

GCT CCA GAT NAA ATG TTT GT;

wherein N is any nucleotide.

17. (Withdrawn) A kit for performing the method of claim 1, comprising penicillin sensitivity-specific DNA probes for determining penicillin sensitivity in *Streptococcus pneumoniae* selected from the group of sequences consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13 and sequences which differ from said sequences by one to four nucleotides, wherein SEQ ID NOS.: 1-13 are, respectively:

AGT CAG CAA CGG GTA AG,

AAC GAA CGA TGG ACG GT,

CAT TTC CAG NCC CCT CCA,

TGC AGA TGC CAC GAT TC,

CTG GTC AGC TTC CTG CG,

TGG TTA TCT AGT CGG GTT AA,  
CTG TAT CGA TGA GTC CG,  
AAC AGT TCT GCT GAA GAA G,  
TAG GAG CAC GCC ATC AGT,  
GAC GAA ATG CCT ATC TTG,  
CTC TCA ATT TGT AGC ACC T,  
CTA TTC TAA CCG TCT GAC A, and  
ATC AAA TAC CTA TAT GGT CC;

wherein N is any nucleotide;

and further comprising penicillin resistance-specific DNA probes for determining penicillin resistance in *Streptococcus pneumoniae* selected from the group of sequences consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19 and sequences which differ from said sequences by one to four nucleotides, wherein SEQ ID NOS.: 14-19 are, respectively:

TGG AGA ATA NTT CAA TAG N,  
GTC TAC TTG AAC AAA AAA TG,  
TTA GTT GGG ACG GAC CCT,  
GTA ACN NTT CAA CAG CCT,  
CTC CGA NCA ATA CGT CTC T, and  
GCT CCA GAT NAA ATG TTT GT;

wherein N is any nucleotide.

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (Previously Presented) The method according to claim 11, wherein the probes are labeled radioactively.

22. (Currently Amended) The method according to claim 8, wherein the DNA sequence of the DNA probes ~~that specifically hybridizes specific~~ to DNA sequences specific for a PBP gene of penicillin sensitive strains of *Streptococcus pneumonia* consists of a DNA sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13 and sequences which differ from said sequences by one to four nucleotides.

23. (Currently Amended) The method according to claim 8, wherein the DNA sequence of the DNA probes ~~that specifically hybridizes specific~~ to DNA sequences specific for a PBP gene of penicillin resistant strains of *Streptococcus pneumonia* consists of a DNA sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19 and sequences which differ from said sequences by one to four nucleotides.

24. (New) A method for testing *Streptococcus pneumoniae* for resistance to penicillin, the method comprising the steps of:

a) isolating DNA from *Streptococcus pneumoniae*, having unknown resistance to penicillin

b) hybridizing the DNA obtained in step (a) with

- (i) more than one oligonucleotide that hybridizes to DNA sequence specific to a penicillin binding protein (PBP) gene of penicillin sensitive strains of *Streptococcus pneumoniae*, wherein this DNA sequence is present in the PBP gene of penicillin sensitive strains of *Streptococcus pneumoniae* but is modified in the DNA sequence aligned thereto of the PBP gene of penicillin resistant strains of *Streptococcus pneumoniae*; and
  - (ii) more than one oligonucleotide that hybridizes to a DNA sequence specific to a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae*, wherein this DNA sequence specific to a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae* is different from the DNA sequence aligned thereto in the PBP gene of penicillin sensitive strains of *Streptococcus pneumoniae* and
- c) determining whether or not said *Streptococcus pneumoniae* is sensitive to penicillin by detecting which oligonucleotide or oligonucleotides hybridize, wherein the PBP gene is selected from the group consisting of PBP2x, PBP1a and PBP2b.

25. (New) The method according to claim 24, wherein the hybridization is carried out under stringent conditions at 20°C below the melting point of the DNA probes.

26. (New) The method according to claim 24, wherein the hybridization is carried out in SSC hybridization solution at a hybridization temperature of 45°-60 °C for at least 5 hours.